OBJECTIVES: Switzerland's regulation of prices for reimbursed drugs is based on referencing across countries and within the therapeutic class for products with comparators. The SwissHTA initiative involving all key stakeholders in the health care systems (sickness funds, industry, physicians, academia, Kantons) has published consensus papers for new benefit criteria and measurements. **METHODS:** A comparison was executed comparing the new proposed criteria against benefit assessments in HTA systems in Germany and the UK. **RESULTS:** In terms of clinical benefit assessment the suggestion by SwissHTA follows accepted evidence-based methods. In comparison to Germany the Swiss approach suggests a pragmatic application by applying disease specific standards. This disease focus allows also accepting different levels of evidence given the characteristics of the disease. This pragmatic approach allows Swiss decision-makers accepting lower evidence levels at the time of launch (e.g. in case of comparison with non-Swiss standard-of-care) coupled with a post-reimbursement commitment. The Swiss method looks similar to the medical benefit application by NICE. In terms of health economic (HE) evaluations SwissHTA suggests focusing on technical efficiency instead of QALY comparisons across the whole system as in the UK. Such an approach avoids the application of arbitrarily defined cost-effectiveness thresholds. In Germany the HE focus is solely based on cost comparisons. In terms of decision-making in Germany the focus is based on an assessment of the available evidence against a theoretical maximum standard of evidence. In the UK coverage decisions are based on cost-effectiveness assessments allowing for context-specific adjustments. In the SwissHTA recommendation a multi-criteria decision-making should be applied with an equal focus on all key aspects (e.g. clinical benefit, public relevance, social preferences, etc.). **CONCLUSIONS:** In comparison to HTA systems in Germany and UK the SwissHTA recommendations seems to be more pragmatic and would follow a broader multi-criteria decision making approach.

PHP154

PRODUCT QUALITY ASPECT IN REIMBURSEMENT OF MEDICAL DEVICES: COMPARISON OF TURKEY VERSUS EUROPE

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OBJECTIVES: FDA has long recognized that dramatic increase in adverse event reports due to medical devices and recalls may reflect quality flaws. While some of this increase can be explicated by FDA's greater outreach emphasizing reporting requirements, failures in product design and manufacturing process cause more than half of all product recalls. Therefore, FDA's concern regarding low quality products remains. In the EU, medical device pre-market quality is assured by CE mark authorization. This regulation is the prerequisite for market registration also for Turkey. However, due to heterogeneity and complexity of devices, manufacturers, imported devices and multiple use environments, there is strong need for post-market quality assurance. **METHODS:** This study investigates whether post-market quality assurance (measured by less adverse events/better health outcomes) can be applied through local reimbursement policies. First, it is investigated whether there are reimbursement rules in Europe acting as post-market quality assurance. Then, a comparison is made with Turkey's existing reimbursement scheme. **RESULTS:** Our comparative analysis reveals only Belgium and France implement quality or brand based reimbursement rules. In Turkey, there is no quality based reimbursement scheme; however current reimbursement application guideline requirements may act as a gate keeper for lower quality products. Our Results show in addition to pre-market regulations, post-market quality can be assured by local reimbursement authorities. **CONCLUSIONS:** There are several opportunities to improve quality assurance and reduce risk across medical device industry; i.e. enhancing visibility of comparative quality to harness market forces and increasing the collaboration between stakeholders. From health policy perspective, implementation of new value based reimbursement models require providers to prove that they're meeting quality standards and benefitting patients while cutting costs. Therefore, while value based payment contracts are still in their infancy in Europe and Turkey, they will have a direct impact on the assurance of continued medical device quality.

PHP155

A COMPARISON OF FACTORS INFLUENCING REIMBURSEMENT AND COVERAGE DECISIONS IN SCOTLAND (SMC), THE NETHERLANDS (NZI) AND GERMANY (G-BA)

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OBJECTIVES: In Germany, Scotland and the Netherlands, the manufacturer's submission is assessed by the HTA bodies; G-BA, SMC and NZi. In Germany, the submitted evidence is used to assess the drug's additional benefit, followed by price-rebate negotiations with the GKV-Spitzenverband. In Scotland and the Netherlands, the submitted evidence is evaluated for reimbursement decision. This study aims to compare factors that influence the reimbursement recommendation by SMC and NZi, the additional benefit by G-BA and the rebate by GKV-Spitzenverband. **METHODS:** Three databases were created consisting of 463 SMC applications, 262 NZi evaluations and 68 G-BA decisions. Logistic regression analyses were conducted to assess the impact of the submitted evidence on the recommendation by SMC and NZi and the effect of variables on the additional therapeutic benefit by G-BA. The impact of variables on the rebate was examined through linear regression analysis. **RESULTS:** In Scotland, 57% of the applications received positive recommendation and the NZi recommended 83% of the submissions. In Germany, 60.3% of the products demonstrated an additional benefit. In Scotland, the multivariate analyses showed that the performance of a cost-minimization analysis and beneficial cost-effectiveness outcomes were the strongest positive predictors of the recommendation. In the Netherlands, univariate analyses showed that the decision was significantly affected by whether the product under assessment was a life-saving intervention and the inclusion of (positive) economic evidence. In Germany, univariate analyses demonstrated that the therapeutic indication and the overall survival benefit, along with improved morbidity and adverse events meaningfully influenced the benefit assessment. Analysis showed that the rebate was significantly reduced by 13% for products that demonstrated additional benefit. **CONCLUSIONS:** Even though reimbursement submission requirements of Scotland and the Netherlands look similar, SMC weights the cost-effectiveness outcomes more, while NZi focuses on the variables related to additional clinical benefit; variables that also significantly influence G-BA's decision.

PHP156

A COMPARISON OF ADDITIONAL BENEFIT SCORES IN GERMANY (GBA) AND FRANCE (HAS)

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OBJECTIVES: The Pharmaceutical Market Restructuring Act (AMNOG) has brought a sustainable change to the reimbursement of new drugs in Germany. The G-BA assesses the additional benefit of the drug, compared to an appropriate therapy. AMNOG law is perceived to be one of the toughest drug evaluation process in Europe. In France the high authority for health (HAS) assesses the level of improvement of actual benefit (IAB). The objective of this study was to compare the additional benefit score issued under AMNOG law to IAB scores granted by the HAS. **METHODS:** All G-BA's additional benefit scores until June 1st 2014 and HAS IAB score were compared. **RESULTS:** In Germany, a total of 76 completed early benefit assessments. From the best available score perspective, the G-BA assessed the additional benefit as considerable in 20% of drugs assessed (score 2), as minor in 30% of drugs assessed (score 3), as unquantifiable in 8% of drugs assessed (Score 4) and as none in 38% of drugs assessed (Score 5). No drug has been granted a major additional benefit (score 1) and 4% of drugs were directly allocated to a reference price group. In France, the transparency committee granted a major improvement in 0.2% of cases (IAB I), an important improvement in 1.3% of cases (IAB II), a moderate improvement 2.5% of cases (IAB III), a minor improvement in 9,2% of cases (IAB 4) and no clinical improvement in 86.8% of cases (IAB V). **CONCLUSIONS:** This study shows that the G-BA assigned an additional benefit (scores from 1 to 4) to more than half of drugs whereas the HAS granted an additional benefice rating to less than 14% of case. This study suggests that there is a more favourable benefit rating in Germany than in France.

PHP157

HTA STATUS OF BIOSIMLARS ACROSS THE UK AND IRELAND

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OBJECTIVES: Biosimilars have the potential to revolutionise the health care landscape by realising cost savings over originator biologics and thus increasing access to innovative medicines. The biosimilars marketplace in the UK and Ireland is relatively new, however the landscape is rapidly developing. The objective of this analysis was to map the HTA status of biosimilars in the UK and Ireland to provide insight for stakeholders involved in the assessment of new biosimilars. **METHODS:** The HTA status of all EMA authorised biosimilars was identified by searching the websites of all four HTA agencies in the UK and Ireland, namely, NICE, the SMC, the AWMSG, and the NCPE. All previously assessed medicines and on-going technology appraisals were screened for the inclusion of biosimilars using the non-proprietary (common name) and proprietary (brand) names. **RESULTS:** Sixteen (84%) of the nineteen biosimilars submitted to the EMA have been authorised, eleven of which (69%) have been considered by HTA agencies. The SMC has approved 100% of the biosimilars it has considered (n=7); the largest positive reimbursement rate amongst all HTA agencies considered. The AWMSG has considered the largest number of biosimilars (n=11), of which five, (45%) received a positive reimbursement status. Both NICE and the NCPE have approved one biosimilar, however three additional biosimilars are currently being considered by NICE. **CONCLUSIONS:** The reimbursement status of biosimilars in the UK and Ireland is not consistent across HTA agencies. The timing of HTA submissions to different HTA agencies may play an important factor in the reimbursement status of biosimilars given that this landscape is relatively new and assessment processes vary. Marketing authorisation holders for biosimilars may want to consider the strategic importance of submitting evidence to each of the HTA agencies in the UK and Ireland, and the impact timing may have on the uptake of their biosimilar.

PHP158

DOES NOT REACHING AN AGREEMENT ON THE FINAL NICE SCOPE HAVE ANY IMPACT ON THE FINAL APRAISAL OUTCOME?

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OBJECTIVES: Identifying the right patient population, comparator and endpoints is key to increase the likelihood of reimbursement. Manufacturers do not always agree with payers' views on these items. Disagreement may lead to funding rejection. We assessed the rate of mismatches between manufacturers and NICE and their impact on the final appraisal outcome. **METHODS:** All manufacturer submissions (MS) from January 2011 until June 2014 were reviewed. For these submissions, the initial proposed scope, the manufacturer's comments, and the final scope and appraisal outcome were analysed. All changes to the initial scope suggested by the manufacturer were recorded and their impact on final outcome investigated. **RESULTS:** In the time period reviewed there were 101 MS of which 7 were suspended and not included in our analysis, while comments were not available for another 18. Manufacturer comments are published for 76 MS. The manufacturer disagreed on ≥1 section of initial scope in 93% (71/76) of MS. The areas where manufacturers and NICE disagreed most commonly are the comparator(s) (43/71; 61%) and population (40/71; 56%) to be assessed. The final scope implemented all and some of the manufacturer's comments in 56% (40/71) and 28% (29/71) of submissions, respectively.

Rejection was more common for manufacturer's comments on outcomes (6/8; 75%) and comparators (8/13; 61.5%). Rate of final recommendation by NICE was higher for those MS where all (29/40; 74%) or certain changes (14/20; 74%) requested by the manufacturer were implemented in the final scope than for those where NICE rejected all manufacturer requests (7/11; 64%), and similar to overall recommendation rate (66/91; 73%). **CONCLUSIONS:** These data highlight that the initial scope frequently does not meet manufacturer's expectations. However, manufacturer's suggestions are often incorporated in the final scope. NICE not implementing manufacturer's suggestions to the final scope does not decrease the likelihood of being granted funding.

PHP159

AN EXAMINATION OF THE REGULATORY AND REIMBURSEMENT PROCESSES FOR BIOBETTERS AND COMPARISON WITH BIOSIMILARS

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OBJECTIVES: Biosimilars and biobetters are subsequent versions of licensed innovator biotherapeutics. Whereas biosimilars are comparable to the originator product in terms of quality, safety and efficacy, biobetters incorporate intentional modifications to the originator molecular profile with the aim of producing a superior product. This distinction between biosimilars and biobetters has important implications from a regulatory perspective, with biosimilars following class-specific guidance whereas biobetters are considered innovator drugs. This study sought to examine and compare the regulatory and reimbursement approaches to the appraisal of biobetters and biosimilars. **METHODS:** Biobetters and biosimilars of the same product class were identified, and qualitative analyses of the recommendations by indication, evidence considered, and key decision drivers were undertaken using available regulatory and HTA reimbursement decision documentation from six European countries. **RESULTS:** Findings for filgrastim are presented as an example; 7 *biosimilars*, and the pegylated filgrastims (pegfilgrastim and lipegfilgrastim) considered *biobetters*, were identified. Biosimilar filgrastims were granted European marketing authorisation based on demonstration of clinical comparability to the originator filgrastim in one indication and extrapolation of the results to all 5 approved indications. Pegfilgrastim demonstrated clinical non-inferiority to filgrastim in one indication and was approved solely for this indication; the subsequently developed lipegfilgrastim was approved for the same indication but used pegfilgrastim as the comparator. Similar to biosimilar filgrastims, economic evidence in the form of cost-minimisation analyses was considered in HTA recommendations of both pegylated filgrastims. This differs from the approach for certain other biobetters that have demonstrated clinical superiority and cost-effectiveness versus their originator. **CONCLUSIONS:** Biosimilars and biobetters are subject to distinct regulatory processes and the decision driving factors for reimbursement also differ among currently licensed biobetters. With the development of these products gaining momentum, it will be interesting to observe how the appraisal processes evolve to address the scope and variety of emerging biobetters.

PHP160

TIME LIMITS RESTRICTION IN GERMANY

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OBJECTIVES: In Germany, with the introduction of the Pharmaceutical Market Restructuring Act (AMNOG) in January 1st2011, pricing and reimbursement decisions for new drugs have been driven by the early benefit assessment (EBA). G-BA can decide to set or not a time limitation to the decision. The objectives of this study were, first, to review the number of time-limited decisions over time and second, to identify drivers of these decisions. **METHODS:** G-BA's decisions, from the introduction of AMNOG Law to June 1st2014, were reviewed. Exempted and/or cancelled procedures were excluded. **RESULTS:** As of June 1st 2014, 76 EBAs were concluded and time limits, from 1 to 5 years, were imposed on 28% (21/76) of these decisions. Short-term restrictions (≤2 years) accounted for 52% (11/21) of the time-limited decisions and long-term (>2 years) for 48% (10/21). Time-limited decisions concerned largely oncology drugs (62%; 13/21), followed by endocrine/metabolic drugs (19%; 4/21) and neurology drugs (10%; 2/21). The number of time limited decisions increased over the studied period, from none (0/2) of the decisions in 2011 to 16% (3/19) in H1 2012, 38% (3/8) in H2 2012, 20% (3/15) in H1 2013, 35% (7/20) in H2 2013 and reaching 42% (5/12) from January 1st to June 1st 2014 decisions. Time-limited decisions were triggered by one or several factors, with safety concerns being the major driver (38%; 8/21). Other drivers were uncertainties of outcomes (33%; 7/21), ongoing studies (33%; 7/21), lack of data (24% (5/21), European Medicine Agency's (EMA) conditional approval (19%; 4/21), design uncertainty (10%; 2/21), inappropriate comparator (10%; 2/21), quality of life concerns (10%; 2/21), and EMA requirements for post-authorisation studies or risk management plan (10%; 2/21). **CONCLUSIONS:** An increasing trend for time-limited decisions was observed. Time restricted decisions have become a major uncertainty management tool in Germany.

PHP161

REIMBURSEMENT TRENDS AND EVIDENCE REQUIREMENTS FOR ULTRA-ORPHAN THERAPIES ACROSS EUROPE: OPTIMISING MARKET ACCESS IN INCREASINGLY CHALLENGING MARKETS

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OBJECTIVES: Ultra-orphan diseases are extremely rare conditions many of which are severe, chronic, and progressive with high mortality rates. There is a growing number of therapies for ultra-rare diseases currently on the market. Reimbursement decisions for these therapies have been characterized by reduced evidence requirements with unmet need weighing heavily into health technology assessment (HTA) and reimbursement decision-making; as well as a generally wide pricing latitude. To gain insight into evolving market access requirements, we conducted a review of pan-European ultra-orphan therapy HTA requirements and reimbursement decisions. **METHODS:** Applying the National Institute for Health and Care Excellence (NICE) definition for ultra-orphan diseases (prevalence of ≤ 1/50,000), full European HTA reports on ultra-orphan therapies published through May 2014 were identified and reviewed to compare evidence requirements and reimbursement decisions across countries for health economic, clinical, and value based criteria. **RESULTS:** Over sixty published ultra-orphan HTAs were identified across nine markets. A small portion of these submissions were rejected for reimbursement largely due to lack of evidence on clinical benefit. For therapies recommended with access restrictions, payers often requested additional follow-on studies or ongoing monitoring of patients by manufacturers. With respect to economic evidence evaluation, reimbursement decisions predominately hinged on therapy cost per patient per year, rather than cost-effectiveness. More recent assessments also evaluated quality of life evidence and input from patient groups. **CONCLUSIONS:** As health care budgets become more strained, ultra-orphan therapies priced at a premium have come under increased scrutiny from HTA agencies and payers to demonstrate value for money. In order to achieve optimal market access, manufacturers must consider continually evolving stakeholder evidence requirements and develop clinical and health economic value plans that demonstrate how their ultra-orphan therapies provide health gain instead of disease stabilization.

PHP162

GLOBAL HTA ASSESSMENTS OF ULTRA-ORPHAN PRODUCTS: A CASE STUDY OF ECULIZUMAB (SOLIRIS) AND IDURONATE-2-SULFATASE (ELAPRASE)

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OBJECTIVES: Ultra-orphan diseases affect a very small patient population, defined by the National Institute for Health and Care Excellence (NICE) as those diseases with a prevalence of ≤ 1: 50,000. Medicines for these indications are difficult to develop in part due to challenges associated with recruiting for clinical trials from a small patient population. Within this context, global payer bodies have assessed these therapies with modified evidence requirements and opportunity for very high prices. We performed a health technology assessment (HTA) review of two ultra-orphan products – eculizumab/Soliris and iduronate-2-sulfatase (IDS)/Elaprase – to gain insight into the evolving HTA evidence requirements for ultra-orphan medicines and comparatively evaluate key decision drivers across geographies. **METHODS:** We scanned global HTAs published before end of May 2014 to identify the two most widely assessed ultra-orphan therapies that have variable reimbursement decision outcomes (eculizumab/Soliris and IDS/Elaprase). To evaluate pivotal decision drivers, we analyzed HTAs across several criteria, including clinical efficacy, unmet need, strength of evidence, cost-effectiveness and burden of illness. **RESULTS:** We identified HTAs in seven countries. For both products, reimbursement decisions varied across agencies. Key decision drivers included cost-effectiveness, clinical efficacy, risk-sharing schemes, and lowered evidence requirements/ special criteria for ultra-orphan medicines. Assessments rejecting Soliris and Elaprase (e.g., Australia, Canada, UK) did so based on cost-effectiveness and lack of long-term survival data. Notably, the NICE Highly Specialized Technology Committee requested unprecedented justification of Soliris pricing. Some agencies (e.g, Scottish Medicines Consortium [SMC]) preemptively rejected the products due to manufacturer non-submission of required data. In Australia, Soliris gained recommendation alongside a risk-sharing scheme while Elaprase gained recommendation under Life Saving Drugs Program criteria. **CONCLUSIONS:** Eculizumab and IDS are among a select list of therapies commanding very high prices globally. This study demonstrates variability in decision criteria and approaches across HTA agencies for such high-priced ultra-orphan products.

PHP163

EVIDENCE-BASED MARKET ACCESS VALUE RESOURCE: NAVIGATING THE HURDLES FOR A BIOLOGIC OBTAINING A LICENSE IN A SECOND INDICATION IN KEY EUROPEAN COUNTRIES

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OBJECTIVES: Market access for an innovative technology, such as a biologic obtaining a license in a second indication, can be complex and time consuming. Reimbursement is critical to rapid adoption of and optimal patient access to a new technology. This study aimed to determine the best approach for communicating value and providing field-based staff with value resources to facilitate dialogue with stakeholders in various scenarios. **METHODS:** We conducted desktop research of published literature, health technology assessment reports, clinical trials data, and third-party websites to identify the critical path and data most valuable to reimbursement decision making in order to prepare a communication resource. We conducted a country-affiliate workshop and qualitative one-on-one interviews with payer decision makers in several key markets to understand funding flow and the most appropriate means of communicating value to external decision makers. **RESULTS:** The process and restrictions for biologics may be stricter than for other medications because of perceived high cost. There are multiple appropriate access pathways for various settings of care, all with varying requirements and value drivers. It is critical to understand the needs of external decision makers and provide field-based staff with a consistent yet customizable means of communicating the value of new technologies. All evidence and insights were synthesized into an evidence-based market access value resource for key stakeholder